EXHIBIT 2

To
Memorandum In Support of TriPath Imaging, Inc.'s Motion to Exclude Defenses Based on Cytyc's CDS-1000

Civil Action No. 03-11142 [DPW] - Lead Case

Filed May 5, 2005

CONTAINS CONFIDENTIAL INFORMATION SUBJECT TO PROTECTIVE ORDER

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

CYTYC CORPORATION, Plaintiff, v. TRIPATH IMAGING, INC., Defendant.	Civil Action No. 03-11142-DPW [Consolidated Action – Lead Case]
TRIPATH IMAGING, INC., Plaintiff, v. CYTYC CORPORATION, Defendant.	Civil Action No. 03-12630-DPW

EXPERT REPORT OF DR. TREVOR JACKSON DARRELL
ON INVALIDITY OF U.S. PATENT NO. 5,715,327

I. Background

1. I have been retained as an expert in this case by counsel for plaintiff. I expect to testify at trial regarding the matters set forth in this report, if asked.

A. Summary Of Report

2. I understand that the defendant, Tripath, Inc., has asserted that Cytyc's ThinPrep Imaging System infringes all claims of U.S. Patent No. 5,715,327 ("the '327 patent"), entitled "METHOD AND APPARATUS FOR DETECTION OF UNSUITABLE CONDITIONS FOR AUTOMATED CYTOLOGY SCORING."

Prescreening Device on Polylysine-Prepared Slides," Analytical and Quantitative Cytology, vol. 3 no. 2, 117-20 (1981) at 117 (Cerviscan is an experimental low-speed interactive prescreening system designed to detect in a specimen any cells with an abnormally high integrated optical density (I.O.D.) nucleus. . . . [A]n autofocus and focus checking module was included in the software, enabling specimens to be scanned completely automatically."); CDS-1000 Source Code, C0143370, CDS-1000 Cytology WorkStation Operator's Manual, C0103065-C0103215, CDS-1000 Image Analysis Algorithms, C0094001-16 (The CDS-1000, a biological specimen slide processing system, includes focus checking software routines, such as FindFocus.c and SpecProc.c, that evaluates whether an image is properly focused.)

24. Based on the prior art references set forth above, including both Tucker articles, it is my opinion that techniques for determining whether a slide processing system has suitably processed a biological specimen were known in the art prior to the filing of the '327 patent application.

2. Uncited Prior Art Teaches A Technique for "Determining Whether A Specimen Collection Result Is Suitable For Automatic Processing," As Claimed in Claims 7-19 Of The '327 Patent

25. The '327 patent describes three suitability tests that address "specimen collection" as a cause for unsuitability. Those tests include (i) percentages of images focused properly on a first try, (ii) percentage of images never focused properly, and (iii) detected intermediate cell ratios. (at Col. 5, lines 47-67 and Col. 6, lines 1-42).

26. As described above, techniques for determining whether or not an image has been focused properly were widely known in the art at the time of filing of the '327 patent. Further, techniques for detecting intermediate cell ratios were also widely known in the art at the time of

filing of the '327 patent. Prior art references not cited during prosecution of the '327 patent disclose determining intermediate cell counts and calculating ratios of intermediate cells to other populations. See, e.g., Tanaka, N., Hideo, I., *et al.*, "Fundamental Study of Automatic Cytoscreening for Uterine Cancer: IV. Sample Requirement for CYBEST and Simulation Test of Cell Dispersion," ACTA Cytologica, Vol. 21, No. 4 (1977) at 534 ("Example A indicates that the number of cells was approximately 200 in the field of view, corresponding to 130 cells per mm^2 with almost equal proportions of the three different types of cells, i.e., 68 cells each of superficial, intermediate, and parabasal cells." The "proportion" of intermediate cells with respect to a total population defines an intermediate cell ratio.); Tanaka, N., Hideo, I., *et al.*, "CYBEST-CDMS: Automated Cell Dispersion and Monolayer Smearing Device for CYBEST," Analytical and Quantitative Cytology, Vol. 3, No. 2, 96-102 at 99 (1981) (The quality of cell dispersion was assessed from the number of isolated cells, the total number of cells and ratio of isolated cells per total cell number in 1 sq mm.); Zahniser, D.J., *et al.*, "Contextual Analysis and Intermediate Cell Markers Enhance High Resolution Cell Image Analysis for Automated Cervical Smear Diagnosis," Cytometry 12: 10-14 at 13 (1991) (Table 3 provides an intermediate cell count and a total count for all cells studied, normal and abnormal); CDS-1000 Source Code, C0143370, CDS-1000 Cytology WorkStation Operator's Manual, C0103065-C0103215 ((The CDS-1000, a biological specimen slide processing system, detects and counts intermediate cells and also counts the total number of cells.)

27. Based on the prior art references set forth above, including both Tanaka articles and the Zahniser article, it is my opinion that techniques for determining whether a specimen collection result is suitable for automatic processing were known in the art prior to the filing of the '327 patent application.

3. Uncited Prior Art Teaches A Technique For "Determining Whether A Slide Handling Result Is Suitable For Automatic Processing," As Claimed In Claims 20-22 Of The '327 Patent

28. One suitability test that the '327 patent describes as a "slide handling" test includes counting saturated image pixels. (at Col. 2, lines 37-39).

29. Techniques for counting saturated image pixels were widely known in the art at the time of filing of the '327 patent. Prior art references not cited during prosecution of the '327 patent disclose counting the number of saturated pixels in an image. *See, e.g.*, U.S. Patent No. 5,282,063 entitled "Method and Apparatus for Automatic Brightness and Contrast Control in an Image Capture System," issued January 25, 1994 (filed August 6, 1992 as a continuation of Ser. No. 368,441, filed June 19, 1989) (at Col. 6, lines 54-58) ("As discussed above, the depicted embodiment of the present invention attempts to locate a black and white level which will result in a selected small number of saturated picture elements, that is, between six and twelve picture elements in the saturated state."; U.S. Patent No. 5,387,896 entitled "Rasterscan Display With Adaptive Decay," issued February 7, 1995, (filed August 6, 1990) (at Col. 6, lines 14-17): "...[I]ndex generator 104 divides the content of register 102 by the content of register 98 to return ratio R of the number of saturated pixels to the number of illuminated pixels."; Dozier, Jeff, "Spectral Signature of Alpine Snow Cover from the Landsat Thematic Mapper," Remote Sens. Environ., 18:9-22 at 11 (1989) ("Plate I identifies saturated pixels in TM Bands 1, 2, and 4 for a typical image, and Figure 1 shows histograms of digital radiance numbers for three dates for these TM bands"); Dozier, at 12, (Caption to Figure 1: "Histograms of digital radiance numbers for TM Bands 1, 2, 4 and 5 for three dates in the southern Sierra Nevada. Top: 24 January 1985. Middle: 25 February 1985. Bottom: 14 April 1985. Also shown are the percentages of saturated pixels in

each band."); CDS-1000 Code at C0143370 (checks the number of saturated pixels in a calibration process).

30. Based on the prior art references set forth above, it is my opinion that techniques for determining whether a slide handling result is suitable for automatic processing were known in the art prior to the filing of the '327 patent application.

4. Uncited Prior Art Teaches An "Intermediate Cell Classifier," As Claimed in Claims 8-17 of the '327 Patent

31. It is my understanding that a true intermediate cell classifier must evaluate, among other cell features, the ratio (N/C) of nuclear area (N) to cytoplasmic area (C) of the cell.[1] Intermediate cell classifiers that evaluated nuclear to cytoplasmic ratios were widely known in the art at the time of filing of the '327 patent. Prior art references not cited during prosecution of the '327 patent disclose such cell classifiers. *See, e.g.*, Zahniser, D.J., *et al.*, "Contextual Analysis and Intermediate Cell Markers Enhance High Resolution Cell Image Analysis for Automated Cervical Smear Diagnosis," Cytometry 12: 10-14 at 11 (1991) ("For the intermediate cell analysis, seven features were selected by the stepwise linear discriminant analysis (Table 1). These included nuclear:cytoplasmic ratio . . . ."); CDS-1000 Cytology WorkStation Operator's Manual, C00103189 ("Intermediate [cells]: Larger than parabasals, still low in N/C ratio . . . ."); Bibbo, *et al.*, "Chromatin Appearance in Intermediate Cells from Patients with Uterine Cancer,"ACTA Cytologica, The Journal of Clinical Cytology, Vol. 25, No. 1, 23-28 at 24 (1981) ("[A] sample of intermediate cells can be readily so classified . . . . The stepwise linear discriminant algorithm was set to select ten features, listed in Table I [including nucleus/cell area ratio] . . . ."); Kwikkel, *et al.*, "Relation of Quantitative Features of Visually Normal Intermediate Cells in Cervical Intraepithelial

41. Tucker I therefore teaches all the elements of and therefore renders obvious claims 5 and 6 of the '327 patent.

B. CDS-1000 Cytology Workstation Anticipates Claims 1-3

42. It is my understanding that, although the CDS-1000 was never a commercial product, it was publicly presented as early as 1992, which was more than one year before the filing date of the '327 patent. (Automated Cervical Cancer Screening – Second Annual Symposium, Georgia International Convention & Trade Center, Atlanta, Georgia C0065268-90).

43. In my opinion, the CDS-1000 Cytology Workstation set forth above (hereinafter CDS-1000) anticipates claim 1 of the '327 patent. Claim 1 recites "[a] method of determining whether a slide processing system has suitably processed a biological specimen slide." The CDS-1000 includes focus checking software routines, *e.g.*, FindFocus.c and SpecProc.c, that evaluate whether an image is properly focused. (C0143370, C0094001-16). Claim 1 further recites "processing the biological specimen slide with the slide processing system." The CDS-1000 acquires and processes images of slide specimens, and analyzes various cell characteristics within the images. (C0103077). Claim 1 further recites "measuring at least one machine processing effectiveness parameter; checking if the at least one machine processing effectiveness parameter has exceeded a limit; and accumulating scan processing error flags." The CDS-1000 focus checking software requires that a certain minimum focus score be reached at least once before any images will be analyzed to determine whether proper focus can be achieved. (C0143370). If the minimum focus score is not reached, then the focus checking software issues an error flag and attempts focus at a position slightly removed from the first field. (C0143370). The CDS-1000 focus checking software accumulates up to four error flags before abandoning the field, and causing the CDS-1000 to stop processing and un-mount the slide. (C0143370). The CDS-1000 includes a "CheckFocus

Error Correction Heuristic" that reviews successive fields on the slide to determine whether each field contains a required minimum number of objects. If not, an error flag is issued. If a predetermined number of error flags is accumulated, the entire slide is rejected. (C0143370, C0094001-16).

44. The CDS-1000 was based on a Macintosh IIx, and ran System Software Version 6.0.5. (C0103174). In my opinion, the Macintosh system software (as well as other operating system software in use at the time of filing the '327 patent) included extensive error handling capability. *See, e.g.*, Ufailure.h routine in the CDS-1000 code. (C0143370). In my opinion, the error handling features of such system software included accumulating error flags that would function as scan processing error flags in the CDS-1000 system. (C0103124).

45. The CDS-1000 Cytology Workstation teaches all the elements of and therefore anticipates claim 1 of the '327 patent.

46. In my opinion, the CDS-1000 also anticipates claim 2 of the '327 patent. Claim 2 adds three limitations to claim 1. The first limitation is "obtaining at least one image of the biological specimen slide." The CDS-1000 captures images of a specimen slide. (C0103077). The second limitation is "processing the at least one image of the biological specimen slide to detect at least one object of interest." The CDS-1000 includes object location programs to locate objects in captured images by sensing contrast differences that distinguish the objects from the background and from other shapes. (C0103106). The third limitation is "scoring the slide as either normal or abnormal based on the at least one object of interest." The CDS-1000 evaluates specimen slides and identifies cells with potential abnormalities. (C0103075).

47. The CDS-1000 Cytology Workstation teaches all the elements of and therefore anticipates claim 2 of the '327 patent.

48. In my opinion, the CDS-1000 also anticipates claim 3 of the '327 patent. Claim 3 adds a limitation to claim 1 that defines one particular way to generate the scan processing error flags, *i.e.*, by "checking if the at least one machine processing effectiveness parameter is within a range." The CDS-1000 includes focus checking software routines, *e.g.*, FindFocus.c and SpecProc.c, that require a certain minimum focus score be reached at least once before any images will be considered for finding a focus peak. The focus cannot be less than zero, so when the CDS-1000 focus checking software determines whether the focus score is below a minimum focus score (to set an error flag), it is also checking to see if the focus score is within a range, *i.e.*, between zero and the minimum focus score.

49. The CDS-1000 Cytology Workstation teaches all the elements of and therefore anticipates claim 3 of the '327 patent.

C. The Second Tucker Article (*Trials with the Cerviscan Experimental Prescreening Device on Polylysine-Prepared Slides,* Analytical and Quantitative Cytology, vol. 3 no. 2, 117-20 (1981)) In Combination With Tucker I Renders Claims 1, 2, 5 And 6 Obvious

50. In my opinion, the Tucker article set forth above (hereinafter Tucker II) renders claims 1, 2, 5 and 6 obvious in view of Tucker I. It is my opinion that one of ordinary skill in the art would have been motivated to combine these articles in that they both describe aspects of the same CERVISCAN cytology system. In fact, Tucker II refers specifically to Tucker I as describing in detail an aspect of the system. (Tucker II, at 120). Specifically, Tucker I describes details of the focusing module referred to in Tucker II. For these reasons, and for the specific reasons set forth below, one would have been motivated to combine the teachings of Tucker I and Tucker II.

intermediate cells, the total cell count, and a proportion of intermediate cells to the total number of cells. (Tanaka I, at 534).

58. Tanaka I teaches all the elements of and therefore anticipates claim 7 of the '327 patent.

E. CDS-1000 Cytology Workstation In Combination With Tanaka I Renders Claims 7, 8, 9, 10, 11, 15 and 16 Obvious

59. In my opinion, claims 7, 8, 9, 10, 11, 15 and 16 are obvious in view of the CDS-1000 Cytology Workstation set forth above ("the CDS-1000") in combination with Tanaka I. It is my opinion that one of ordinary skill in the art would have been motivated to combine the teachings of the CDS-1000 with the teachings of Tanaka I to supply the missing claim elements (*i.e.*, "processing a slide to obtain at least one slide result; measuring at least one specimen collection result parameter; and checking if at least one of the at least one specimen collection result parameters have exceeded a limit") because the techniques for improving sample adequacy taught by Tanaka I (*e.g.*, better cell dispersion) would improve the operation of the CDS-1000.

60. The CDS-1000 does not describe the first three elements of claim 7. However, as set forth above, Tanaka I describes those elements. Claim 7 further recites "identifying a number of objects detected as intermediate cells; identifying a total number of objects detected; and dividing the number of objects detected as intermediate cells by the total number of objects detected to generate an intermediate cell ratio." The CDS-1000 provides a scan results window that displays to the user a number of cellular objects (*i.e.*, the total number of objects that were identified as cells), a number of diagnostic objects (*i.e.*, the total number of potentially abnormal objects), and a number of intermediate objects found during the scan of a specimen slide. (C0103133-34). The CDS-1000 includes the software routine ranknuc.c that combines several cell feature values extracted from the

captured image of the slide specimen variables to determine whether a detected object is an intermediate cell. (C0143370). The CDS-1000 does not explicitly calculate a ratio of intermediate cell count to total cell count. In my opinion, however, calculating a ratio of two numbers is obvious once you have determined the relevant numbers. For example, Tanaka I describes determining a ratio of intermediate cells to total cells. Thus, in my opinion, it would have been obvious to one skilled in the art to take the intermediate cell count and the total cell count of the CDS-1000 and compute an intermediate cell ratio, as taught in Tanaka I.

61. The CDS-1000 in combination with Tanaka I teaches all of the elements of and therefore anticipates claim 7 of the '327 patent.

62. Claim 8 recites all of the limitations of claim 7, but adds the limitation "intermediate cell nuclei are detected by an intermediate cell classifier, and wherein the intermediate cell nuclei has at least one feature value, further including the step of computing a mean of the at least one feature value over all detected intermediate cell nuclei." The CDS-1000 includes the software routine ranknuc.c that defines several variables related to cell features, *e.g.*, ".nucshape" (shape of the nucleus), ".nucarea" (area of the nucleus), ".nuctext" (texture of the nucleus), ".nuciod" (integrated optical density of the nucleus), among others. (C0143370). The CDS-1000 assigns a value to each of these feature variables based on the captured image to produce feature values. (C0143370). The CDS-1000 uses these and other feature values to determine whether an object is an intermediate cell. (C0143370). Thus, the CDS-1000 uses these feature values to classify cells as likely intermediate cells. In my opinion, computing a mean of a set of feature values is obvious once you have determined the values. Thus, in my opinion, it would have been obvious to one skilled in the art to compute a mean of intermediate cell nuclei feature values of the CDS-1000 over all detected intermediate-type cells.

63. The CDS-1000 in combination with Tanaka I teaches all the elements of and therefore renders obvious claim 8 of the '327 patent. One skilled in the art would have been motivated to combine the CDS-1000 with Tanaka I for the reasons set forth above.

64. Claim 9 recites all of the limitations of claim 8, but adds the limitation "a mean optical density for each detected intermediate cell nucleus is calculated and a histogram of all intermediate cell optical densities is created." As described above for claim 8, the CDS-1000 includes the software routine ranknuc.c that defines a variable ".nuciod" (integrated optical density of the nucleus). (C0143370). Integrated optical density of a nucleus is the sum of optical densities calculated over the nucleus, and mean optical density is the sum of optical densities divided by the area of the nucleus. Determining the mean optical density is an obvious extension of the integrated optical density. The CDS-1000 also makes use of histograms (*see, e.g.*, ranknuc.c function "updatehisto()"). (C0143370). In my opinion, it would have been obvious to one skilled in the art to calculate a mean optical density from the integrated optical density already calculated by the CDS-1000 and to create a histogram of the mean optical densities.

65. The CDS-1000 in combination with Tanaka I teaches all the elements of and therefore renders obvious claim 9 of the '327 patent.

66. Claim 10 recites all of the limitations of claim 9, but adds the limitation "computing a standard deviation of mean optical densities for all detected intermediate cell nuclei on the slide." As discussed above for claim 9, the mean optical density is an obvious extension of the integrated optical density generated by the CDS-1000. In my opinion, computing a standard deviation of a set of numbers is obvious once you have determined the set of numbers.

67. The CDS-1000 in combination with Tanaka I teaches all the elements of and therefore renders obvious claim 10 of the '327 patent. One skilled in the art would have been motivated to combine the CDS-1000 with Tanaka I for the reasons set forth above.

68. Claim 11 recites all of the limitations of claim 8, but adds the limitation "calculating an average feature value for all detected intermediate cell nuclei on the slide and calculating a mean of an optical density in an area produced by finding a dilation residue minus a closing of a nuclear mask for each detected intermediate cell nucleus." As discussed above with respect to claim 8, the CDS-1000 determines a number of feature values and uses those feature values to determine whether an object is an intermediate cell. (C0143370). In my opinion, computing an average of a set of numbers is obvious once you have determined the set of numbers. Thus, in my opinion it would have been obvious to calculate an average feature value for all detected intermediate cell nuclei detected by the CDS-1000. The CDS-1000 also performs dilation and closing operations in routines such as BinMorph.c. (C0143370). In my opinion, morphology operations were standard image analysis tools at the time of filing the patent application, and morphology operations such as those used in BinMorph.c were well known to those skilled in the art. Such morphology operations were also commonly used to perform image classification. A mask is well known to be a binary rendering of a grayscale image. Further, dilation and closing were well-known editing procedures for binary images at the time of filing of the patent application. *See, e.g.*, "Computer Assisted Microscopy, The Measurement and Analysis of Images," John C. Russ, Department of Materials Science and Engineering, College of Engineering, North Carolina State University, Chapter 6 at 5, 9 and 16 (1988); and the CDS-1000 routines such as BinMorph.c. (C0143370). A "dilation residue" is the result of dilating an image. Thus, in my opinion it would have been obvious to (i) find a

dilation residue of a nuclear mask, (ii) subtract a closing of the nuclear mask from the dilation residue so as to define an area, then (iii) calculate a mean of an optical density in that area.

69. The CDS-1000 in combination with Tanaka I teaches all the elements of and therefore renders obvious claim 11 of the '327 patent. One skilled in the art would have been motivated to combine the CDS-1000 with Tanaka I for the reasons set forth above.

70. Claim 15 recites all of the limitations of claim 8, but adds the limitation "dilating the image of each detected intermediate cell to generate a dilated image." As discussed above for claim 11, dilation was a basic editing procedure for binary images well known to those skilled in the art at the time of filing the patent application. *See, e.g.*, "Computer Assisted Microscopy, The Measurement and Analysis of Images," John C. Russ, Department of Materials Science and Engineering, College of Engineering, North Carolina State University, Chapter 6 at 5, 9 and 16 (1988); and the CDS-1000 routines such as BinMorph.c. (C0143370). Thus, in my opinion it would have been obvious to dilate the image of each intermediate cell detected by the CDS-1000.

71. The CDS-1000 in combination with Tanaka I teaches all the elements of and therefore renders obvious claim 15 of the '327 patent. One skilled in the art would have been motivated to combine the CDS-1000 with Tanaka I for the reasons set forth above.

72. Claim 16 recites all of the limitations of claim 8, but adds the limitation "computing a residue image by subtracting the original image from the dilated image." As discussed above for claim 11, dilation was a basic editing procedure for binary images that were well known in the art at the time of filing the patent application. *See, e.g.*, "Computer Assisted Microscopy, The Measurement and Analysis of Images," John C. Russ, Department of Materials Science and Engineering, College of Engineering, North Carolina State University, Chapter 6 at 5, 9 and 16

(1988); and the CDS-1000 routines such as BinMorph.c. (C0143370). Thus, in my opinion it would have been obvious to dilate the image of each intermediate cell detected by the CDS-1000. Further, in my opinion, subtracting one image from a dilated image was well known in the art at the time of filing the patent application and is, thus, an obvious editing procedure. For binary images, subtraction may be effected via exclusive OR-ing the images. *See, e.g.*, "Computer Assisted Microscopy, The Measurement and Analysis of Images," John C. Russ, Department of Materials Science and Engineering, College of Engineering, North Carolina State University, Chapter 6 at 3 (1988).

73. The CDS-1000 in combination with Tanaka I teaches all the elements of and therefore renders obvious claim 16 of the '327 patent. One skilled in the art would have been motivated to combine the CDS-1000 with Tanaka I for the reasons set forth above.

F. The Second Tanaka Article (*CYBEST-CDMS Automated Cell Dispersion and Monolayer Smearing Device for CYBEST,*" Analytical and Quantitative Cytology, Vol. 3, No. 2 (1981)) In Combination With Tanaka I Renders Claim 7 Obvious

74. In my opinion, claim 7 is obvious in view of the Tanaka article set forth above (hereinafter Tanaka II) in combination with Tanaka I. It is my opinion that one of ordinary skill in the art would have been motivated to combine these articles in that they both describe aspects of the CYBEST automated cytoscreening and image analysis system. In fact, Tanaka II refers explicitly to Tanaka I (Tanaka II, at 102). Further, Tanaka II describes preparing slide specimens with improved cell dispersion and overlap characteristics. One would have been motivated to combine the teachings of Tanaka I and Tanaka II, since doing so would improve the performance of the automated cell analyzer described in Tanaka I.

calculate a ratio of intermediate cell count to total cell count. In my opinion, however, calculating a ratio of two numbers is obvious once you have determined the relevant numbers. For example, as set forth above, Tanaka I describes determining a ratio of intermediate cells to total cells. Thus, in my opinion, it would have been obvious to one skilled in the art to take the intermediate cell count and the total cell count of Zahniser and compute an intermediate cell ratio, as taught in Tanaka I, because doing so improves the statistical information with respect to intermediate cells.

80. Zahniser in combination with Tanaka I teaches all the elements of and therefore renders obvious claim 7 of the '327 patent.

H. Tucker I In Combination With Either (i) Tanaka I, (ii) Tanaka II In View Of Tanaka I, (iii) The CDS-1000 In View Of Tanaka I, Or (iv) Zahniser In View Of Tanaka I, Renders Asserted Claims 18 And 19 Obvious

81. Claim 18 recites all of the limitations of claim 7, and adds the limitation of "calculating at least one percentage of images acquired in focus on at least one predetermined number of tries." This limitation is not described in any of the combinations set for above for rendering claim 7 invalid. However, from Tucker I, issuing a focus error flag causes the focus correction routine to automatically rescan the field "at a series of different z axis positions to find the position of maximum integrated optical density. Interlocks are provided to prevent cycling on fields which contain insufficient image content." The focus monitor routine "prints a digital 'map' of the focus position for each scanned field, and at which autofocus scans were requested." (Tucker I, at 235-36). This digital map includes focus position information for each scanned field, particularly, the positions where the system focused on a first try and the positions where an autofocus was requested. Further, it is my opinion that the map would necessarily include information for every field on the slide where focus was attempted. Thus, the map would also

identify the fields that have insufficient image content for the autofocus function. Tucker I therefore describes all information necessary (*i.e.*, the number of fields where images were acquired in focus and the total number of fields where focus was attempted) to determine the percentage of images acquired in focus. . One skilled in the art would have been motivated to combine Tucker I with either (i) Tanaka I, (ii) Tanaka II in view of Tanaka I, (iii) the CDS-1000 in view of Tanaka I, or (iv) Zahniser in view of Tanaka I to supply the missing claim element because the FOCWATCH focus checking routine of Tucker I would have improved the performance of either the CYBEST or the CDS-1000 automated slide processing systems, and for all of the reasons described above.

82. Tucker I in combination with either (i) Tanaka I, (ii) Tanaka II in view of Tanaka I, (iii) the CDS-1000 in view of Tanaka I, or (iv) Zahniser in view of Tanaka I, teaches all the elements of and therefore renders obvious claim 18 of the '327 patent.

83. Claim 19 recites all of the limitations of claim 7, and adds the limitation of "calculating a percentage of images that were never adequately focused." This limitation is not described in any of the combinations set for above for rendering claim 7 invalid. However, from Tucker I, issuing a focus error flag causes the focus correction routine to automatically rescan the field "at a series of different z axis positions to find the position of maximum integrated optical density. Interlocks are provided to prevent cycling on fields which contain insufficient image content." The focus monitor routine "prints a digital 'map' of the focus position for each scanned field, and at which autofocus scans were requested." (Tucker I, at 235-36). This digital map includes focus position information for each scanned field, particularly, the positions where the system focused on a first try and the positions where an autofocus was requested. Further, it is my opinion that the map would necessarily include information for every field on the slide where focus was attempted. Thus, the map would identify the fields that have insufficient image content for the

autofocus function. Thus, Tucker I describes all information necessary (*i.e.*, the number of fields where images were never adequately focused and the total number of fields where focus was attempted) to determine the percentage of images that were never adequately focused. One skilled in the art would have been motivated to combine Tucker I with either (i) Tanaka I, (ii) Tanaka II in view of Tanaka I, (iii) The CDS-1000 in view of Tanaka I, or (iv) Zahniser in view of Tanaka I to supply the missing claim element because the FOCWATCH focus checking routine of Tucker I would have improved the performance of either the CYBEST or the CDS-1000 automated slide processing systems, and for all of the reasons described above.

84. Tucker I in combination with either (i) Tanaka I, (ii) Tanaka II in view of Tanaka I, (iii) CDS-1000 in view of Tanaka I, or (iv) Zahniser in view of Tanaka I, teaches all the elements of and therefore renders obvious claim 19 of the '327 patent.

I. The Tucker Articles, Separately In Combination With U.S. Patent No. 5,282,063 Renders Claims 4, 20 And 21 Obvious

85. Claim 4 recites all of the limitations of claim 1 except for the final limitation regarding accumulating scan processing error flags. Instead, claim 4 adds the limitation of "calculating at least one percentage of images that have more than at least one predetermined number of pixels saturated." This limitation is not described in either of the Tucker articles. As set forth above, both Tucker I and Tucker II disclose a slide processing system for processing a specimen slide. Both Tucker articles describe a mechanism in the CERVISCAN automated cytology system for rejecting unsatisfactory specimens based on determining if a parameter has been exceeded. Tucker I and Tucker II further disclose that the CERVISCAN system scans each slide using an autofocus and focus-checking module, generating scanner error flags if focus is not achieved on a first try. (Tucker I, at 232, 235; Tucker II, at 117-19). The Tucker articles therefore

V. Conclusions

99. Asserted claims 1-3 of the '327 patent are invalid because they are anticipated by Tucker I. Further, asserted claims 5 and 6 of the '327 patent are invalid because they are obvious in view of Tucker I.

100. Asserted claims 1-3 of the '327 patent are invalid because they are anticipated by the CDS-1000 Cytology Workstation.

101. Asserted claims 1-3, 5 and 6 of the '327 patent are invalid because they are rendered obvious by Tucker II in combination with Tucker I.

102. Asserted claim 7 of the '327 patent is invalid because it is anticipated by Tanaka I. Asserted claim 7 is also invalid because it is obvious in view of Tanaka II, the CDS-1000 or Zahniser, in combination with Tanaka I.

103. Asserted claims 8-11, 15 and 16 of the '327 patent are invalid because they are rendered obvious by the CDS-1000 in view of Tanaka I.

104. Asserted claims 18 and 19 of the '327 patent are invalid because they are rendered obvious by Tucker I in combination with either (i) Tanaka I, (ii) Tanaka II in view of Tanaka I, (iii) the CDS-1000 in view of Tanaka I, or (iv) Zahniser in view of Tanaka I.

105. Asserted claims 4, 20 and 21 of the '327 patent are invalid because they are obvious in view of each of the Tucker articles in combination with the '063 patent, the '896 patent or the Dozier article.